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The University of Chicago
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EFFECTS OF CERTAIN SALTS ON KIDNEY EXCRETION, WITH SPECIAL REFERENCE TO GLYCOSURIA

A DISSERTATION

SUBMITTED TO THE FACULTY OF THE OGDEN GRADUATE SCHOOL OF SCIENCE, IN CANDIDACY FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

(DEPARTMENT OF PHYSIOLOGY)

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EFFECTS OF CERTAIN SALTS ON KIDNEY EXCRETION, WITH SPECIAL REFERENCE TO GLYCOSURIA.[1]

BY ORVILLE HARRY BROWN.

[*From the Hull Physiological Laboratory of the University of Chicago.*]

A TRANSIENT glycosuria occurs under a great number of conditions and is an accompanying symptom of more or less importance in a great variety of maladies. Experimentally it is well known that a transient increase of sugar in the urine can be produced in a variety of ways, chief of which are the use of phlorhizdin, adrenalin chloride, excessive amounts of narcotics, extirpation of the pancreas, a puncture of the fourth ventricle, and by large amounts of sugar taken into the alimentary canal. In marked diuresis sugar is usually found in the urine. Jacobj[2] showed that in rabbits glycosuria always accompanied the diuresis, produced by caffein, caffein sulphate, and theobromine. Bock and Hoffman[3] found sugar in the urine after intravenous injections of large quantities of a 1 per cent solution of sodium chloride. Kessler[4] observed that sugar was constantly in the urine of cats after injections of sodium carbonate.

At the suggestion of Dr. A. P. Mathews, I undertook a series of experiments to ascertain the effect of salt solutions on the production of diuresis, and on the excretion of sugar by the kidneys. If the kidney activities are influenced by ions as are the functions of other

[1] Since this paper has been sent to the Journal, reprints from Dr. MARTIN H. FISCHER, of a preliminary report in the University of California Publications, on "The Production and Suppression of Glycosuria in Rabbits through Electrolytes," have been received. It is certainly gratifying that his results, as far as reported, corroborate mine. I wish to say that practically all of my results were obtained during the winter quarter of 1903, and have been publicly announced several times by Dr. A. P. MATHEWS. See Yale Medical Journal, June, 1903.

[2] JACOBJ: Archiv für experimentelle Pathologie und Pharmakologie, 1895, xxxv, p. 213.

[3] BOCK and HOFFMAN: Archiv für Anatomie und Physiologie, 1871, i, s. 550; JACOBJ: *Loc. cit.*

[4] KESSLER: Versuch uber die Wirkung einiger Diuretics, Dissertation, 1877, Dorpat; JACOBJ: *Loc. cit.*

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tissues of the body, then we have reason to assume that the renal excretion, either in quality or quantity, or both, would be increased by some ions and decreased by others. Dr. A. P. Mathews[1] has shown that nerve fibres are stimulated by anions and depressed by cations. Loeb[2] has shown that the nature of the ions in a solution in which a muscle is immersed has an important influence on the muscle contraction. Cole,[3] and Neilson and Brown[4] have demonstrated that the activities of enzymes and catalytic agents are retarded by cations and accelerated by anions.

Methods.

Rabbits were employed for the experiments. A 6 per cent solution of urethane given by the stomach was used as the anesthetic, $1\frac{1}{2}$ gm. being given per kilo weight. The solutions used were injected into the jugular vein. The urine was collected from a cannula which was inserted into the bladder. The urine was tested for sugar, qualitatively by Haines's[5] solution, fermentation, and the polarimeter, and quantitatively by either Fehling's solution or the polarimeter, or both. As there was always a possibility of sugar's being produced in the urine, by the operation combined with the anesthetic, the solutions were not injected until it had been shown that there was no glycosuria, or in case there was some, until the urine no longer gave a test for sugar. There were but a few experiments where sugar appeared after the operation before the injection of a solution. If it appeared, it usually disappeared within one or two hours.

The experiments given below were repeated a number of times with similar results. In some of the phlorhizdin experiments calcium chloride was used in place of the strontium chloride. It had practically the same effect, but possibly had a greater tendency to decrease the amount of water excreted. There is, however, a depression of water excretion by both the calcium and strontium chlorides when they are used in sufficient quantities. In a number of cases complete or nearly complete anuria was produced by suddenly increasing the

[1] Mathews: Science, N. S., 1903, No. 436, p. 729.

[2] Loeb: This journal, 1900, iii, p. 383.

[3] Cole: Journal of physiology, 1903, xxx, p. 281.

[4] Neilson and Brown: This journal, 1904, x, p. 225.

[5] Haines's solution is the same as Fehling's solution except that the copper sulphate and alkali are kept together, with sufficient glycerine added to dissolve the copper hydrate.

amount of calcium or strontium chloride injected. This tendency toward suppression of the kidney excretion was much more marked with one lot of rabbits which was used than with the rest. The explanation for this I do not know. Dr. S. A. Matthews[1] has observed that anuria can be produced by the use of an $\frac{m}{8}$ solution of gold chloride. In smaller amounts he has found that the gold chloride inhibits the excretion of sugar produced by those salts which produce diuresis. It was also observed during the course of my experiments that sodium acetate, sodium citrate, and barium chloride caused a very active peristalsis which in some cases resulted in the defecation of a large amount of watery fæces. It should be observed that sodium chloride and sodium citrate produce a reducing substance in the urine, even though the amount of urine excreted was in some cases very much less than the amount of the solution injected. This substance in the first few experiments was tested only by the use of Haines's solution. The reduction, however, resembled closely that resulting from a known sugar, placed in sugar-free urine.

Experiment 1. — Rabbit, weight, 2500 gms. 10 c.c. urine in 45 minutes. No sugar. 20 c.c. $\frac{m}{8}$ sodium acetate injected slowly. 40 c.c. of urine excreted. This gave a heavy reduction with Haines's solution.

Experiment 2. — Rabbit, weight, 2100 gms. 8.45 to 9.30 A.M., 14 c.c. of urine were collected. No sugar. At 9.30 a slow injection of sodium citrate was begun. Amount excreted was practically equal to amount injected. This urine gave a heavy reduction with Haines's solution.

Experiment 3. — Rabbit, weight, 1880 gms. From 2.00 to 3.00 P.M., 21 c.c. of urine were excreted. No sugar. From 3.00 to 3.20, 16 c.c. of an $\frac{m}{8}$ sodium sulphate were injected. At 4.30, $1\frac{1}{2}$ hours after the beginning of the injection, 43 c.c. of the solution had been injected, and 185 c.c. of urine had been excreted. This urine gave a heavy reduction with Haines's solution.

Experiment 4. — Rabbit, weight, 1700 gms. From 9.00 to 10.00 A.M., 10 c.c. of urine were collected. No glycosuria. From 10.00 to 12.00, 20 c.c. of $\frac{m}{8}$ sodium chloride were injected. 40 c.c. of urine collected. Heavy reduction of Haines's solution was produced by this urine.

Experiment 5. — Rabbit, weight, 1900 gms. The urine following the operation gave a marked reduction of Haines's solution. After $1\frac{1}{2}$ hours this had disappeared. During the next hour a mixture of 50 c.c. $\frac{m}{8}$ sodium

[1] Personally communicated.

chloride, 25 c.c. $\frac{m}{8}$ sodium sulphate, and 25 c.c. $\frac{m}{8}$ sodium citrate, was injected. 87 c.c. of urine were collected, and sugar was shown by Haines's solution and fermentation to be present in considerable quantities.

Experiment 6. — Rabbit, weight, 1700 gms. Reducing substance in urine, after the operation. From 10.00 to 12.00 injected 100 c.c. of an $\frac{m}{8}$ solution of sodium chloride. This urine produced considerable gas on fermentation, and gave a heavy reduction with Haines's solution. From 12.00 to 1.30, 97½ c.c. of $\frac{m}{8}$ sodium chloride and 2½ c.c. of $\frac{m}{8}$ calcium chloride were injected. 27½ c.c. of urine were collected, and on fermentation only a small amount of gas was given off, and on treating with Haines's solution only a slight precipitate was produced. From 1.30 to 3.00, 95 c.c. of sodium chloride and 5 c.c. of $\frac{m}{8}$ calcium chloride were injected. 50 c.c. of urine were excreted. Neither fermentation nor reduction of Haines's solution took place.

Experiment 7. — Rabbit, weight, 1500 gms. 8 c.c. of urine from 10.00 to 11.00. No sugar. This experiment was the same as 6, except strontium chloride was substituted for calcium chloride. The sugar which was produced by the sodium chloride was prevented by the addition of small amounts of strontium chloride to the sodium chloride. The specific gravity of urine was 1.016 during the sodium chloride injection, and 1.005 after the addition of the strontium chloride. From 3.00 to 5.00, injected 200 c.c. of a mixture[1] of sodium chloride, sulphate, and citrate, in the proportion of 50 c.c. of an $\frac{m}{8}$ solution of the first, 25 c.c. of an $\frac{m}{4}$ solution of the second, and 25 c.c. of an $\frac{m}{12}$ solution of the third. 275 c.c. of urine were removed. 0.005 gm. of sugar per c.c. of urine were shown by Fehling's solution to be present. From 5.00 to 7.00 P.M., injected 200 c.c. of a solution the same as the one mentioned just preceding, except that in 100 c.c. of the mixture, there were 45 c.c. of sodium chloride instead of 50 c.c., 22½ c.c. of sodium citrate instead of 25, and 7½ c.c. of $\frac{m}{8}$ strontium chloride was added. 130 c.c. of urine were excreted. By the same test as above, 0.002 gm. of sugar per c.c. of urine were shown to be present. The last few c.c. of urine collected gave no sugar test.

Experiment 8. — Rabbit, weight, 1710 gms. No sugar in urine following the operation. Injected slowly a mixture of 50 c.c. of $\frac{m}{8}$ sodium chloride, 25 c.c. of $\frac{m}{4}$ sodium sulphate, 20 c.c. of $\frac{m}{12}$ sodium citrate, and 5 c.c. of $\frac{m}{8}$ calcium chloride. Test for sugar in urine excreted was negative.

[1] This, with a small amount of $\frac{m}{8}$ calcium chloride, is the combination used by Dr. S. A. Matthews for producing diuresis and successfully applied by him in the treatment of tetanus.

Experiment 9. — Rabbit, weight, 1330 gms. Given a subcutaneous injection of 5 c.c. of a 2 per cent alcoholic solution of phlorhizdin. Sugar was found in the urine after 20 hours.

Experiment 10. — Rabbit, weight, 1540 gms. No sugar an hour after operation. From 11.30 to 1.30, 80 c.c. of $\frac{m}{8}$ sodium chloride and 20 c.c. of $\frac{m}{8}$ strontium chloride were injected. At 12.00, 5 c.c. of phlorhizdin, the same solution as used above, was given subcutaneously. At 2.00, 50 c.c. of urine were excreted. No glycosuria. The flow of urine became very slow, and 50 c.c. of an $\frac{m}{8}$ sodium chloride were injected, and by 6.00 o'clock, 30 c.c. of urine had been excreted. Just a very slight reduction occurred when treated with Haines's solution.

Experiment 11. — Rabbit, weight, 1300 gms. No sugar in urine for an hour after operation. From 10.30 A.M. to 12.30 P.M., a mixture of a 95 c.c. of $\frac{m}{8}$ sodium chloride, and 5 c.c. strontium chloride, and 5 c.c. of the phlorhizdin as used before, was injected. Samples of urine collected up to 12.30 A. M. gave only in two or three cases slight traces of sugar.

Experiment 12. — Rabbit, weight, 1570 gms. At 9.15 there was a slight amount of reducing substance. None at 10.45. At 10.45, injected 25 c.c. of an $\frac{m}{8}$ solution of sodium chloride. At 12.30, 27 c.c. of urine were excreted. No sugar. At 12.30, injected 25 c.c. sodium chloride and $\frac{1}{2}$ c.c. phlorhizdin. Within about 15 minutes sugar was found in the urine. By 2.45, 30 c.c. of urine were excreted, the last samples of which contained no sugar. The urine, tested quantitatively by the polariscope, showed that 0.2 gm. of sugar were excreted. My readings of the polariscope were verified in every case by Dr. Guthrie. At 3.00 injected 24 c.c. of $\frac{m}{8}$ sodium chloride and $\frac{1}{2}$ c.c. of phlorhizdin, same as before used. By 5.20, 26 c.c. of urine had been excreted, the last of which contained no sugar. The amount of sugar excreted this time, tested in the same manner as before, was 0.05 gm.

Summary and Conclusions.

1. An $\frac{m}{8}$ solution of sodium chloride, an $\frac{m}{8}$ solution of sodium citrate, an $\frac{m}{8}$ solution of sodium acetate, and an $\frac{m}{8}$ solution of sodium sulphate, as observed by Dr. S. A. Matthews[1] and others, and corroborated by my experiments, produces diuresis.

2. These same salts, as has been observed by Mock and Hoffman[2] in case of sodium chloride, produce a glycosuria.

[1] Dr. S. A. Matthews: Personally communicated.

[2] Mock and Hoffman: *Loc. cit.*

3. It might seem that the diuresis was the cause of the glycosuria, except that by an addition of small amounts of calcium or strontium chloride, the glycosuria is prevented while the diuresis still exists.

4. Calcium and strontium chlorides likewise decrease or totally inhibit the excretion of sugar which is caused by the injection of phlorhizdin.

5. Since diuresis and glycosuria are caused by those salts which have been found by Dr. A. P. Mathews[1] to stimulate nerve, and that depression of these activities is caused by salts which he has found to depress the irritability of nerve, we may assume that the anions stimulate the renal activities, and the cations depress them.

6. It was not ascertained whether the glycosuria caused by the salts was the same as that produced by phlorhizdin, or whether the sugar of the blood was increased. Further experiments are being carried on in this laboratory to determine this, and to ascertain the practical value of results obtained.

I take this opportunity to express my thanks to the members of the laboratory, especially Dr. A. P. Mathews and Dr. S. A. Matthews.

[1] Dr. A. P. Mathews: *Loc. cit.*

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